Presence of antimicrobial pharmaceutical residues in various environmental compartments in selected Finnish, Kenyan and Zambian sites

➔ Pius Kairigo*
PhD student, MSc
University of Jyväskylä,
Department of Biology and
Environmental Science,
Jyväskylä, Finland,
pius.k.kairigo@jyu.fi

➔ Cecilia Muriuki
PhD student, MSc
Jomo Kenyatta University of
Agriculture and Technology,
Department of Soil, Water
and Environmental Engineering,
Nairobi, Kenya

➔ Elijah Ngumba
Lecturer, PhD
Jomo Kenyatta University of
Agriculture and Technology,
Department of Chemistry,
Nairobi, Kenya

➔ James Raude
Senior Lecturer, PhD,
Jomo Kenyatta University of
Agriculture and Technology,
Department of Soil, Water and
Environmental Engineering,
Nairobi, Kenya

➔ Anthony Gachanja
Professor, PhD,
Jomo Kenyatta University of
Agriculture and Technology,
Department of Chemistry,
Nairobi, Kenya

➔ Tuula Tuhkanen
Professor, PhD
University of Jyväskylä
Department of Biology and
Environmental Science,
Jyväskylä, Finland

*Correspondence

ABSTRACT

The occurrence of antibiotics and antiretroviral drugs in the aquatic environment is becoming a major concern due to their potential in the propagation of antimicrobial resistance and possible toxicity to aquatic organisms. In this study, selected pharmaceuticals most relevant in the management of HIV/AIDS, tuberculosis and other opportunistic ailments, including three antiretroviral drugs (nevirapine, zidovudine and lamivudine) and seven antibiotics (trimethoprim, sulfamethoxazole, ciprofloxacin, norfloxacin, tetracycline, doxycycline and amoxicillin), were analyzed in untreated (influent) and treated (effluent) municipal wastewater, effluent suspended matter, surface water, river sediments, groundwater and source separated urine in Finland, Kenya, and Zambia.

The study revealed widespread contamination of surface water in Kenya and Zambia with the concentration of the measured pharmaceuticals several orders of magnitude higher than in Finland. The mean concentrations in treated municipal wastewater ranged between 0.016 and 0.54 µg/L in Jyväskylä, 0.08 to 55.8 µg/L in Lusaka and 0.066 to 4 µg/L in Nairobi. Mean surface water concentrations of the studied pharmaceuticals in Jyväskylä were only up to 0.054 µg/L, whereas the concentration in Nairobi and Lusaka were several magnitudes higher with the peak concentrations of 13.8 µg/L and 49.7 µg/L, respectively. In addition, pharmaceuticals were detected in the treated wastewater suspended particulate matter (SPM) at concentrations between 11 µg/kg to 31117 µg/kg. The impact of the flow of SPM was evident in the river sediments since river sediment samples collected downstream of the effluent discharge point had four times higher concentration compared to samples collected upstream. This underpins the importance to consider the SPM phase as a significant pathway to the emission of residual pharmaceuticals from the wastewater treatment plant. In Lusaka, pharmaceuticals were also analyzed in groundwater and source separated urine. The compounds were only sporadically present in groundwater with concentration ranging from below detection limit to peak at 880 ng/L. However, high concentrations up to several mg/L were measured in source separated urine with 7.7 mg/L, 12.8 mg/L and 10 mg/L for sulfamethoxazole, trimethoprim and lamivudine, respectively.

Preliminary risk assessment based on the comparison of measured environmental concentration (MEC) to the compound-specific predicted no effect concentrations for resistance selection ($PNEC_{(RS)}$) values was conducted. Finnish samples had low to medium risk while the Kenyan and Zambian samples had medium to high risk for resistance selection. The high concentrations measured in Kenya and Zambia are a direct consequence of the direct discharges of untreated waste into the environment, high disease burden which translates to increased consumption of pharmaceuticals, high population density, insufficient sewer line connectivity and the poor treatment efficiencies of the wastewater treatment plants. The high concentration of pharmaceuticals in the source separated urine (SSU) is an indicator of the great potential of source separation as a critical barrier to environmental contamination.

Keywords: Antibiotics, antiretroviral drugs, antimicrobial resistance, wastewater, suspended particulate matter, sediments

INTRODUCTION

Organic micropollutants of pharmaceutical nature are environmental contaminants of concern. Occurrence of residual active pharmaceutical ingredients (API's) in environmental compartments, including the waste waters, surface waters, sediments, suspended solids, manure and soils across the globe have been reported (Lindberg *et al.* 2014, Segura *et al.* 2015, aus der Beek *et al.* 2016, Carvalho and Santos 2016, Hanna *et al.* 2018, Lin *et al.* 2018, Madikizela *et al.* 2020,). One of the most important pathways of environmental contamination by APIs is through the excretion of consumed pharmaceuticals that pass through the wastewater treatment process or by the direct discharge of untreated excreta. Other sources include the disposal of unused medicines, veterinary medicines, effluents from the manufacturing process, and the use of sewage sludge as fertilizers (Kümmerer 2008, Kümmerer 2009, Hughes *et al.* 2013). Since excreted pharmaceuticals are a major contributor to the environmental loading, the wastewater collection and treatment systems in an area will largely determine the extent of environmental contamination by APIs.

Urine contributes approximately 1% by volume of the total wastewater (Spångberg *et al.* 2014, Barbosa *et al.* 2019), but consists up to 99% of the active ingredient and the metabolites of ingested pharmaceuticals. Pharmaceutical consumption within the low and middle-income countries is increasing. This is because of the existing high disease burden. For instance, treatment of tuberculosis and management of HIV/AIDS patients through antiretroviral therapy leads to consumption of tons of medication (WHO 2016), for which a good percentage ends up into the environment as parent compounds or active metabolites.

The ubiquitous detection of APIs in the hydrological cycles is an issue of great concern. This is because presence of the sub-inhibitory concentrations of antimicrobials within the aquatic environment increases the selection pressure for the evolution of antimicrobial resistance within the environmental bacteria (Andersson and Hughes 2014, Khan *et al.* 2017). Antimicrobial resistance is a global threat to public health.

In this study, untreated and treated wastewater, suspended particulate matter in the wastewater and surface water, river sediments and source separated urine samples, were collected from sites in Kenya, Zambia and Finland for analysis of selected antibiotics and antiretroviral drugs. The present study reveals that contamination of water bodies by APIs is extensive in the developing countries such as Kenya and Zambia as compared with Finland and with that reported in other studies carried out in developed countries. Risk for the evolution of antimicrobial resistance within the aqueous samples in the environment based on compound specific predicted no effect concentrations for resistance selection ($PNEC_{(RS)}$) is also reported.

Table 1. Use, dosage and percentage excretion rates as unchanged parent compound for selected antibiotics and antiretroviral drugs (Ngumba *et al.* 2020).

Compound	Use	Typical Dose (mg/d)	Treatment period (days)	Excretion rate as unchanged compound (%)
Sulfamethoxazole (SMX)	Antibiotic	1600	5 or daily	15–25
Trimethoprim (TMP)	Antibiotic	320	5 or daily	80–90
Ciprofloxacin (CIP)	Antibiotic	500	5	80
Norfloxacin (NOR)	Antibiotic	800	5	60
Doxycycline (DOX)	Antibiotic	100	8	70
Tetracycline (TET)	Antibiotic	1000	10	80–90
Amoxicillin (AMO)	Antibiotic	1500	7	60–80
Zidovudine (ZDV)	Antiretroviral	600	Daily	15–20
Lamivudine (3TC)	Antiretroviral	300	Daily	70
Nevirapine (NVP)	Antiretroviral	400	Daily	2.7

Table 2. Summary of the samples taken and the collection locations. GW: Groundwater; SSU: Source separated urine; SW: Surface water; WWE: Wastewater effluent, treated wastewater; WWI: wastewater influent, untreated WW; WSPs: waste stabilization ponds, WWTP: Wastewater treatment plant.

	Location	Sample type	No of samples	Sampling time
Kenya	Nairobi	SW-grab	40	October 2014,
	Nyeri	SW-grab	36	January & September 2019
	Machakos	SW-grab	24	January & September 2019
Zambia	Chunga/Madimba residential areas	GW-grab	27	June 2016
	Chunga River	SW-grab		June 2016
	Matero WSPs	WWI/WWE-grab	6	June 2016
	Chunga/Madimba residential areas	SSU-grab	20	June 2016
Finland	Jyväskylä WWTP	WWI/WWE-composite 24h	4	September 2015, March 2016
	Lake Päijänne	SW-grab	6	March 2016
	Lake Jyväsjärvi	SW-grab	6	October 2014
	Hiedanranta, Tampere	SSU- grab	4	August 2019

MATERIALS AND METHODS

Studied pharmaceuticals

The pharmaceuticals analyzed in the study, and their percentage excreted as parent compound are listed in **Table 1**.

Study area and sample collection

The samples were collected in selected municipalities in Kenya, Zambia and Finland as indicated in **Table 2**. Kenya and Zambia represented the developing countries while Finland represented developed countries.

The samples were prepared as described in the previous studies (Ngumba *et al.* 2016, Ngumba *et al.* 2020). In brief, the method involves concentration and clean-up step by solid phase extraction followed by API identification and quantification by liquid chromatography tandem mass spectrometry using positive mode electrospray ionization (LC-ESI-MS/MS). The sediment and suspended particulate matter (SPM) samples were prepared by the ultrasonic bath extraction and stepwise sample extraction operations as described in our earlier publications (Kairigo *et al.* 2020b, Muriuki *et al.* 2020). Results for SPM and river sediments were reported on the dry weight basis.

Risk assessment for evolution of antimicrobial resistance

The compound-specific $PNEC_{(RS)}$ values, whose calculation factored multiple genera of pathogenic microorganisms present in the environment as proposed by Bengtsson-Palme and Larsson (2016), was used to assess the risk for evolution of antimicrobial resistance by the selected antibiotics in the surface waters. The risk quotient (RQ) was calculated based on equation 1.

$$RQ = \frac{MEC}{PNEC_{(RS)}} \qquad (1)$$

in which RQ is the risk quotient, MEC the measured environmental concentration in the representative samples, and $PNEC_{(RS)}$ the compound-specific predicted no-effect concentration for resistance selection. RQ ≥1 represents high risk, 1 > RQ ≤0.1 medium risk, and RQ < 0.1 low risk.

RESULTS AND DISCUSSION

Occurrence of selected pharmaceuticals in aqueous and sediment samples

The summary of the measured mean concentrations of the selected APIs monitored in this study in untreated wastewater (influent), treated wastewater (effluent), SPM in treated wastewater, surface water, river sediment, and groundwater, is presented in **Table 3**.

The pharmaceuticals in Kenyan and Zambian samples in some instances occurred at concentrations more than 1000 times higher as compared to concentrations in samples collected in Finland. The big difference in the occurrence of pharmaceutical residues in the environment might mirror the disease burden in the society and the pharmaceutical consumption patterns. A previous study reported lack of proper information on use and disposal of antibiotics especially among the informal settlements in sub-Saharan Africa (Karimi *et al.* 2020). Besides of the suboptimal consumption of medicines, improper disposal practices of unused and expired medicine were reported. Up to 32 % and 10 % of the households (n=447), sampled across five informal settlements, reported disposing of their remainder antibiotic doses in pit latrines and compost pits, respectively.

Besides API residues, retransformation of conjugated metabolites back to parent compounds may occur under favorable conditions within the wastewater treatment process or the natural environment (Polesel *et al.* 2016). For instance, the acetylated (N4-acetyl-SMX) and glucuronide (SMX-N1-Glu, SMX-2′-Glu) metabolites, which are the major metabolites of sulfamethoxazole, undergo deconjugation within the wastewater treatment process, which results to negative removal efficiencies within wastewater treatment plants (WWTPs) (Radke *et al.* 2009). Such deconjugation may also explain the increased amounts of the parent compounds in wastewater effluents compared with influents, which was also observed in this study (**Table 3**).

In groundwater samples in Zambia, the levels of SMX, CIP, TMP, AMO and NVP ranged from 0.14 to 0.66 µg/L (**Table 3**). These levels were comparable with those reported in other parts of the world (**Table 4**) and in some occasions higher. The ground water wells sampled in Zambia could explain the higher occurrence rates due to the leaching effect resulting from the close proximity to the pit latrines and compost pits.

It is clear that the developing countries have higher prevalence of environmental pharmaceutical residues than developed countries. Aqueous samples dominate many studies, and the occurrence in the solid particulate matter and river sediments is often overlooked. In this study we found that the SPM phase had consistently higher amount of pharmaceutical residue as compared to the effluent wastewater. Calculation of the mass emission of pharmaceuticals from the wastewater treatment plant can therefore be biased without the consideration of the contribution of the SPM phase (Muriuki *et al.* 2020). Therefore, the SPM is an important phase of consideration in the emission of pharmaceuticals in non-conventional wastewater treatment lagoons. The effluent SPM impacts the river sediments downstream the effluent discharge point since higher levels of pharmaceutical residues were measured in the river sediments collected downstream of the effluent discharge point as compared to the upstream samples (Kairigo *et al.* 2020a).

Lack of access to the centralized wastewater treatment systems may also contribute discharge of untreated waste directly to the environment. By the time of sampling, some urban areas in Kenya had less than 10 % of the population connected to the sewer system (KNBS 2019). The concentrations from the Sub–Saharan African region are significantly high in both surface waters and groundwater, which can be attributed to direct discharge of untreated wastewater, discharges from WWTPs, and leaching from pit latrines soak pits and septic tanks. The high concentration of APIs in environment means that the local population are in a close contact with highly contaminated water sources. The contaminated water is used for irrigation, bathing, and other domestic purposes, sometimes even as drinking water. Currently, there are no environmental standards for maximum

Table 3. Mean concentrations of antibiotics and antiretroviral drugs in wastewater treatment plant influent and effluent water, effluent SPM, surface water, and river sediments (abbreviations of APIs in Table 1) (mean±stdev).

API	Country-Location	Influent (µg/L)	Effluent (µg/L)	Effluent SPM (µg/kg)[a,b]	Surface water (µg/L)	River sediments (µg/kg)[a,b]	Ground water (µg/L)
SMX	Finland-Jyväskylä	0.1	0.2	n.a	0.03	na	n.a
	Zambia-Lusaka	33.3	30.0	n.a	11.8	na	0.7
	Kenya-Nairobi	n.a	3.3	n.a	13.8	n.a	n.a
	Kenya-Nyeri	22.5±2.4	10.0	2085±510	4.4±0.8	422.3±46	n.a
	Kenya-Machakos	9.1±1.6	94.2	23448± 1959	142.5± 9	895.6±29	
CIP	Finland-Jyväskylä	0.4	0.1	n.a	0.1	n.a	n.a
	Zambia-Lusaka	0.7	0.2	n.a	0.5	n.a	0.2
	Kenya-Nairobi	n.a	0.1	n.a	0.5	n.a	n.a
	Kenya-Nyeri	9.9± 1.9	6±1.1	31117± 349	6±1.3	290.4±21	n.a
	Kenya-Machakos*	8.1± 1.3	5.4±1.1	5017±344	2.8±0.9	1275.3±30	n.a
NOR	Finland-Jyväskylä	0.2	0.1	n.a	0.1	n.a	n.a
	Zambia-Lusaka	0.1	80	n.a	n.a	n.a	
	Kenya-Nyeri	3.9±0.8	3.6±0.6	12617±712	5.9±0.9	327.6±44	n.a
	Kenya-Machakos*	5.2±1.7	4.2±0.8	82267±559	1.6±0.4	248.32	n.a
TMP	Finland-Jyväskylä	0.6	0.5	n.a	0.1	n.a	n.a
	Zambia-Lusaka	32.7	1.8	n.a	2.4	n.a	0.1
	Kenya-Nairobi	n.a	0.1	n.a	2.6	n.a	n.a
	Kenya-Nyeri	24.6±3	5.3±1.6	1567±419	0.9±0.1	71.7±3.5	n.a
	Kenya-Machakos*	11.32	158±12	3080±845	4.4±0.4	90±6.3	n.a
DOX	Finland-Jyväskylä	0.1	0.02	n.a	n.d	n.a	n.a
	Zambia-Lusaka	4.5	5.3	n.a	3.3	n.a	
TET	Finland-Jyväskylä	0.04	0.03	n.a	nd	n.a	
	Zambia-Lusaka	0.2	4.6	n.a	4.2	n.a	nd
AMO	Finland-Jyväskylä	0.1	0.1	n.a	n.d	n.a	n.a
	Zambia-Lusaka	3.3	5.6	n.a	3.4	n.a	0.7
3TC	Finland-Jyväskylä	0.1	0.02	n.a	0.01	n.a	n.a
	Zambia-Lusaka	119	55.8	n.a	49.7	n.a	n.a
	Kenya-Nairobi	n.a	3.9	n.a	5.4	n.a	n.a
	Kenya-Nyeri	76±8	2±0.4	1131±315	2.8±0.7	27.5±4.7	n.a
	Kenya-Machakos	1463.5±69	847±65	69681±5824	228.3±9	106.6±1.3	n.a
ZDV	Finland-Jyväskylä	0.1	0.04	n.a	nd	n.a	n.a
	Zambia-Lusaka	66.6	37.1	n.a	9.7	n.a	nd
	Kenya-Nairobi	n.a	0.5	n.a	7.7	n.a	n.a
	Kenya-Nyeri	1.9±0.5	3±0.5	2415±505	1.19±0.3	62.6±7.7	n.a
	Kenya-Machakos	4.07±0.6	1.44±0.5	3336±119	1.1±0.2	118±15	n.a
NVP	Finland-Jyväskylä	0.02	0.01	n.a	n.d	n.a	n.a
	Zambia-Lusaka	0.7	1.7	n.a	0.2	n.a	0.04
	Kenya-Nairobi	n.a	1.3	n.a	4.9	n.a	
	Kenya-Nyeri	1.3±0.7	0.9±0.1	2006±133	1.4±0.5	120±27	n.a
	Kenya-Machakos	47.3± 8	9.5±1.3	3214±146	2.2±0.5	100.6±16	n.a

n.a = not analysed; <LOQ= concentration lower than limit of quantification;
n.d = not detected;
a,b = values adapted from (Kairigo *et al.* 2020a, Muriuki *et al.* 2020).

Table 4. Concentrations of selected antibiotics and antiretroviral drugs in wastewater, surface water and ground water from different countries. Results are reported either as mean or as a concentration range (abbreviations of APIs in Table 1).

API	Country	Influent (µg/L)	Effluent (µg/L)	Surface water (µg/L)	Ground water (µg/L)	References
SMX	China	n.r	n.r	0.029	0.0032	Tong *et al.* 2014, Yao *et al.* 2017
	Sweden	0.674	0.304	n.r	n.r	Lindberg *et al.* 2005
	Spain	n.r	n.r	n.r	0.065	López-Serna *et al.* 2013
	USA	n.r	n.r	n.r	0.113	Schaider *et al.* 2014
	Kenya	54.83	4.09	39.00	0.030	K'oreje *et al.* 2016
	South Africa	59.28	1.6	8.7	n.r	Agunbiade and Moodley 2014, Matongo *et al.* 2015a, 2015b
	India	0.220	0.260	n.r	n.r	Subedi *et al.* 2017
	Africa	n.r	n.r	2.53	n.r	aus der Beek *et al.* 2016
CIP	Spain	n.r	n.r	n.r	0.44	López-Serna *et al.* 2013
	South Africaw	27.1	14.1	14.3	n.r	Agunbiade and Moodley 2016
	Vietnam	<MDL – 3.035	n.r	n.r	n.r	Tran *et al.* 2019
	Finland	4.23	0.13	0.036	n.r	Vieno *et al.* 2006
	Africa	n.r	n.r	0.017	n.r	aus der Beek *et al.* 2016
NOR	China	n.r	n.r	0.278	0.097	Tong *et al.* 2014, Yao *et al.* 2017
	Spain	n.r	n.r	n.r	0.00046	López-Serna *et al.* 2013
	Australia	2.2	2.5	11.5	n.r	Watkinson *et al.* 2009
	Sweden	0.174	0.037	n.a	n.r	Lindberg *et al.* 2005
	France	n.a	n.a	0.16	n.r	Tamtam *et al.* 2008
	Africa	n.r	n.r	0.076	n.r	aus der Beek *et al.* 2016
TMP	China	n.r	n.r	0.019	0.0052	Tong *et al.* 2014
	Spain	n.r	n.r	n.r	0.0094	López-Serna *et al.* 2013
	Kenya	72.85	0.15	7	0.006	K'oreje *et al.* 2016
	USA	n.a	n.a	0.020	0.002	McEachran *et al.* 2016
	South Africa	0.013	0.16	0.87	n.r	Matongo *et al.* 2015a, 2015b
	Mozambique	n.r	n.r	6.223	n.r	Segura *et al.* 2015
	Africa	n.r	n.r	0.985	n.r	aus der Beek *et al.* 2016
DOX	China	n.r	n.r	0.066	0.0642	Tong *et al.* 2014
	Spain	n.r	n.r	n.r	0.188	López-Serna *et al.* 2013
	Australia	0.65	0.15	0.4	n.r	Watkinson *et al.* 2009
	Ghana	n.a	n.a	0.005	n.r	Segura *et al.* 2015
	Sweden	2.48	0.88	n.r	n.r	Lindberg *et al.* 2005
TET	China	n.a	n.a	0.1	0.0252	Tong *et al.* 2014, Yao *et al.* 2017
	South Africa	5.68	1.7	2.8	n.r	Agunbiade and Moodley 2014
	Spain	n.r	n.r	n.r	56.3	López-Serna *et al.* 2013
	Ghana	n.r	n.r	465	n.r	Segura *et al.* 2015
	Kenya	n.r	n.r	434	n.r	Segura *et al.* 2015
	Belgium	1.66	n.d	n.r	n.r	Vergeynst *et al.* 2015
AMO	Australia	6.94	0.050	0.2	n.r	Watkinson *et al.* 2009
	UK	n.r	n.r	0.245	n.r	Kasprzyk-Hordern *et al.* 2007
	Germany	1.27	0.187	n.r	n.r	Rossmann *et al.* 2014
	Vietnam	<MDL - 20.6	n.r	n.r	n.r	Tran *et al.* 2019
	Kenya	0.7	1.24	0.3	n.r	Kairigo *et al.* 2020b
3TC	Kenya	60.68	31.07	167	n.r	K'oreje *et al.* 2016
	South Africa	n.r	n.r	0.132	n.r	Wood *et al.* 2015
	Germany	0.72	n.d	n.d	n.r	Prasse *et al.* 2010
ZDV	Kenya	20.13	0.11	17	0.030	K'oreje *et al.* 2016
	Germany	0.38	0.564	0.17	n.r	Prasse *et al.* 2010
NVP	Kisumu, Kenya	3.3	2.08	5.62	1.6	K'oreje *et al.* 2016
	South Africa	2.1	0.35	1.48	n.r	Mashiane 2015, Wood *et al.* 2015
	Germany	0.0218	0.032	0.013	n.r	Prasse *et al.* 2010

n.r = not reported; n.d = not detected, <MDL = below the method detection limit.

allowable API concentrations in water in the Sub-Saharan African region.

Occurrence of pharmaceuticals in source separated urine

The mean concentrations of the pharmaceuticals in SSU is shown in **Figure 1**. In samples collected at Hiedanranta, Finland, the concentrations ranged between 0.75 µg/L and 8.65 µg/L, whereas the concentrations in samples collected in source separating toilets in Zambia ranged between 1.4 µg/L and 2430 µg/L. SMX was the most abundant pharmaceutical in both locations with concentrations of 8.65 µg/L and 2430 µg/L, respectively, with a difference of almost 300-fold. TMP and 3TC were also abundant in the Zambian urine samples with mean concentrations of 2199 µg/L and 1670 µg/L, respectively. 3TC is a first line antiretroviral drug, whereas the antibiotics, SMX and TMP, are widely used in the management of opportunistic diseases in HIV patients. The abundance of the combination of these drugs in SSU can be used as a pointer of the disease burden in the community. Furthermore, the use of untreated SSU as fertilizer is risky because of the uptake of APIs by food crops (Azanu *et al.* 2018). Lack of proper management of the source separated urine can lead to direct discharge of the untreated urine directly into the water bodies causing contamination to hydrological cycles with elevated levels of API residues especially in places where the rivers have very low volumes and flow rates.

So far, only a few studies on occurrence of antibiotics and antiretroviral drugs in source separated urine exist. A South African study reported concentration ranges of 2-6800 µg/L and 2-1300 µg/L for SMX and TMP, respectively. The study also reported presence of antiretroviral drugs, ritonavir and emtricitabine, at levels ranging from 1 µg/L to 4.6 µg/L and from 6 to 680 µg/L, respectively (Bischel *et al.* 2015). Proper management of urine source separation in a system whereby the separated urine undergoes treatment to eliminate residual pharmaceuticals can be an effective barrier to control environmental pollution from human point sources, while retaining essential plant nutrients such as nitrogen and phosphorus (Solanki and Boyer 2017).

Risk for evolution of antibiotic resistance in the environment

Selection of antimicrobial resistance occur in the environment, when the microbial organisms are exposed to antimicrobials in sub-lethal doses. In these conditions, the resistant bacteria have selective advantage and undergo enrichment (Gullberg *et al.* 2011). The proposed compound specific predicted no effect concentration ($PNEC_{(RS)}$) reported in the literature can be found for selected antibiotics including NOR (0.5 µg/L), CIP (0.064 µg/L), TMP (0.5 µg/L), SMX (16 µg/L), DOX (2 µg/L), and AMO (0.25 µg/L) (Bengtsson-Palme and Larsson 2016). The concentrations of these pharmaceuticals reported in the surface waters in this study are of great concern, since they occur above the proposed threshold values for the evolution of antimicrobial resistance. The risk quotients ranged from 0.001 to 93.5, as illustrated in **Figure 2**, indicating there is medium to high risk for evolution of antimicrobial resistance within the sampled environments. CIP (RQ=93.8), NOR (RQ=11.8), and AMO (RQ=13.6) accounted for the highest risks in this study in surface water samples collected in Kenya and Zambia. Samples from Finland had low to medium risk with risk quotients ranging between 0.001 and 0.7.

A recent study by our research group reported medium to high risk for resistance selection within the river waters and WWTP effluents (Kairigo *et al.* 2020b). Furthermore, the synergistic effects of residual pharmaceuticals may be amplified in the environment, where they occur as cocktails, whose synergistic toxicity may be elevated compared with that ascertained for individual compounds.

The threat for evolution of resistant bacteria under these environmental concentrations are real. Multidrug resistant tuberculosis is already an issue of concern in Africa and Asia (WHO 2017). Besides antimicrobial resistance, our research group has previously reported ecotoxic effects to aquatic organisms (Ngumba *et al.* 2016).

CONCLUSION

In general, the concentrations of the selected pharmaceuticals detected in Finland were low and thus environmental and health risks posed by the pharmaceuticals are relatively low as well. However, the concentrations measured in Kenya and Zambia were several orders of magnitude higher. In the developing countries, pharmaceutical residues primarily emanate from the direct discharge of untreated wastewater and effluents from wastewater treatment plants. Prevention of direct flow of untreated waste water is a control barrier that is chronically missing in areas with higher prevalence of pharmaceutical resi-

dues in the environment. For instance in the sampling sites in Finland (Jyväskylä), there exists a centralized conventional waste water treatment plant with secondary wastewater treatment that serves a known number of people. In areas with informal settlements, such accuracy is not possible.

Therefore, the use of improved sustainable sanitation solutions that conclusively accounts for proper collection, treatment and disposal of excreta can mitigate direct discharge of untreated waste directly into the urban hydrological cycles. The high concentration of APIs measured in source separated urine was an indicator of the great potential of source separation as a critical barrier to environmental contamination. The source separation, treatment and disposal of the excreta at least of the patients under constant and heavy medication could allow the use of urine as a fertilizer without risk of pharmaceutical contamination. Improved sanitation would also enhance the efficient nutrient recycling in a closed-loop fertility cycle after the proper collection and the residual treatment of the APIs. Overall, in order to protect human and environmental health, there is a need to establish critical control points throughout the lifecycle of APIs.

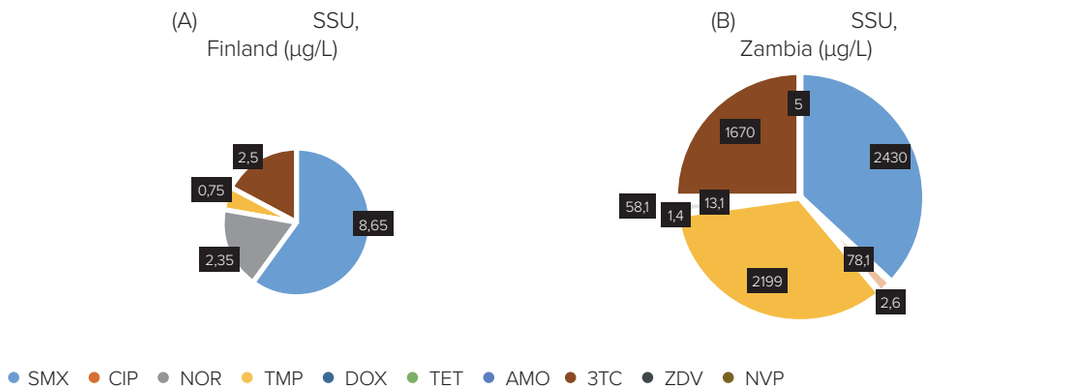

Figure 1. Occurrence of selected antibiotics and antiretroviral drugs in source separated urine samples collected in (A) Hiedanranta, Tampere Finland and (B) Lusaka, Zambia (abbreviations of APIs in Table 1).

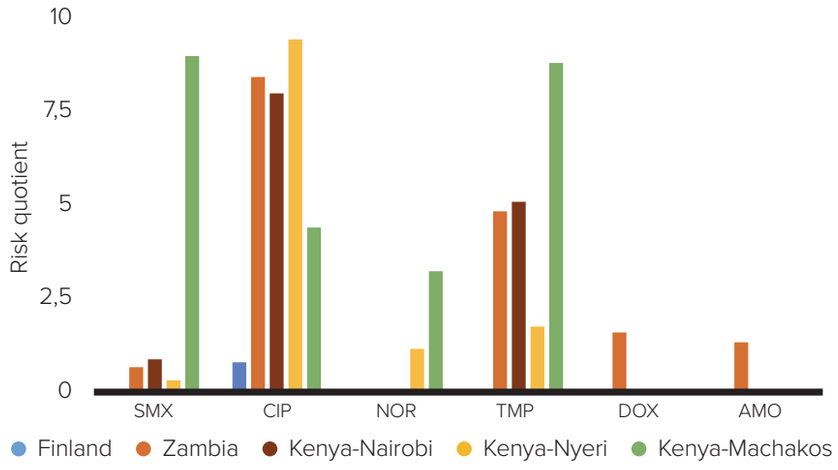

Figure 2. Risk quotient for evolution of antimicrobial resistance in surface waters. RQ ≥1 =high risk, 1 > RQ ≤ 0.1 = medium risk and RQ < 0.1 = low risk (abbreviations of APIs in Table 1).

TIIVISTELMÄ

Antimikrobisten lääkejäämien esiintyminen ympäristönäytteissä Suomessa, Keniassa ja Sambiassa

➔ Pius Kairigo*
Tohtorikoulutettava, MSc
Jyväskylän yliopisto,
Biologian ja ympäristötieteiden laitos,
Jyväskylä, Suomi,
pius.k.kairigo@jyu.fi

➔ Cecilia Muriuki
Tohtorikoulutettava, MSc
Jomo Kenyatta University of Agriculture and Technology, Department of Soil, Water and Environmental Engineering,
Nairobi, Kenia

➔ Elijah Ngumba
Lehtori, PhD
Jomo Kenyatta University of Agriculture and Technology, Department of Chemistry,
Nairobi, Kenia

➔ James Raude
Vanhempi lehtori, PhD
Jomo Kenyatta University of Agriculture and Technology, Department of Soil, Water and Environmental Engineering,
Nairobi, Kenia

➔ Anthony Gachanja
Professori, PhD,
Jomo Kenyatta University of Agriculture and Technology, Department of Chemistry,
Nairobi, Kenia

➔ Tuula Tuhkanen
Professori, FT
Jyväskylän yliopisto,
Biologian ja ympäristötieteiden laitos,
Jyväskylä, Suomi

*Kirjeenvaihto

Antibioottien ja antiviraalisten lääkeainejäämien esiintymisen ympäristössä on havaittu muodostavan ongelman niiden aiheuttamien ekotoksikologisten vaikutuksien ja mahdollisen antibioottiresistenssin muodostumisen takia. Tässä työssä mitattiin eräitä tuberkuloosin ja AIDS/HIV:n hoidossa käytettäviä antibiootteja (trimetopriini, sulfametoksatsoli, siprofloksasiini, tertasyksiini, doksimysiini, norfloksasiini ja ampisilliini) ja antiretroviraalisia lääkeaineita (nevirapiini, zidovudiini ja lamivudiini) käsittelemättömästä ja käsitellystä yhdyskuntajätevedestä, pinta- ja pohjavesistä sekä jäteveden kiintoaineesta ja vastaanottajavesistöjen sedimenteistä Suomessa, Keniassa ja Sambiassa.

Keniasta ja Sambiasta otettujen näytteiden lääkeainepitoisuudet olivat useita kertaluokkia suurempia kuin Suomesta kerättyjen näytteiden pitoisuudet. Jyväskylän käsitellyn jäteveden keskimääräiset pitoisuudet vaihtelivat välillä 0,016–0,54 µg/l, Lusakassa välillä 0,08–55,8 µg/l sekä Nairobissa välillä 0,066–4,0 µg/l. Keskimääräiset pintavesien lääkeainepitoisuudet olivat Jyväskylässä enimmillään 0,054 µg/l, mutta Nairobissa jopa 13,8 µg/l ja Lusakassa 49,7 µg/l. Myös käsitellyn jäteveden mukana karkaava kiintoaine sisälsi runsaasti lääkeaineita. Pitoisuudet vaihtelivat välillä 11–31 117 µg/kg. Jätevesiä vastaanottavien jokien sedimentin lääkeainepitoisuudet olivat purkupaikan alapuolella keskimäärin neljä kertaa suurempia kuin ennen purkupaikkaa. Jäteveden sisältämällä kiintoaineella on merkittävä osuus lääkeaineiden kulkeutumisessa ympäristöön. Lusakasta tutkittiin myös pohjavesinäytteitä ja kokoomanäytteitä virtsaa erittelevistä käymälöistä. Pohjaveden lääkeainepitoisuudet vaihtelivat alle määritysrajan olevalta tasolta aina 880 ng/L tasolle. Erilliskerätty virtsa sisälsi lääkeaineita yhteensä useita milligrammoja litraa kohti. Korkeimpina pitoisuuksina esiintyi sulfametaksatsolia (7,7 mg/l), trimetopriimia (12,8 mg/l) ja lamivudiinia (10,0 mg/l).

Vertaamalla antibioottien pintavesissä mitattuja pitoisuuksia (engl. measured environmental concentration, MEC) kirjallisuudessa esitettyihin yhdistekohtaisiin pitoisuuksiin, jotka eivät aiheuta painetta antibioottiresistenssin muodostumiselle (engl. predicted no-effect concentration for resistance selection PNEC(RS)), voidaan todeta, että riski antibioottiresistenssin muodostumiselle Suomessa on matala, mutta Keniassa ja Sambiassa jopa erittäin suuri. Vähemmän kehittyneissä maissa jätevesien ja ympäristön korkeat lääkeainepitoisuudet johtuvat virtsan ja ulosteen päätymisestä käsittelemättömänä suoraan

ympäristöön, keskitetyn keräily- ja käsittelyjärjestelmän puutteista, suuresta väestötiheydestä ja tautikuormasta. Erityisen korkeita lääkeainepitoisuuksia mitattiin virtsan erilliskeräykseen tarkoitetuista käymälöistä. Näin ollen erilliskeräys, käsittely ja loppusijoitus olisivat erittäin tehokkaita tapoja vähentää lääkeaineiden ympäristökuormitusta.

Avainsanat: Antibiootit, antiretroviraaliset lääkeaineet, antimikrobiresistenssi, jätevesi, kiintoaine, sedimentti

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CONFLICTS OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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